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PROVISIONAL APPLICATION COVER SHEET

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This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53(b)(2).

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TITLE OF THE INVENTION (280 characters max)

FERROELECTRIC FILMS FOR BIOLOGICAL SENSING AND DETECTION APPLICATIONS

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ENCLOSED APPLICATION PARTS (check all that apply)

- ☒ Specification 6 pages — Small Entity Statement ________
- ☒ Drawing(s) 2 Sheets — Other (specify)

METHOD OF PAYMENT (check one)

☒ A check or money order is enclosed to cover the Provisional filing fees ☒ Applicant(s) claim small entity status ☒ The Commissioner is hereby authorized to charge any additional fees and credit any overages to Deposit Account Number: 04-1577	Provisional filing fee amount(s)	$ 80.00

Respectfully submitted,

Signature: ____________ Date: January 30, 2004

Typed or Printed Name: Ralph A. Dowell Registration No.: 26,868

Ferroelectric films for biological sensing and detection applications

FIELD OF THE INVENTION

The present invention relates to the application of ferroelectric films for biological sensing and detection.

BACKGROUND OF RELATED ARTS

Biosensors, which associate a biological component with known transducers, are becoming increasingly important bioanalytical tools in medicine and the development of industrial activities, particularly in automation, regulation, quality control and energy conservation.

Biosensors can be classified based on the transduction methods they employ. A great variety of transduction methods have been utilized for biosensors in the last two decades. Most forms of transduction can be categorized in the following three main classes: optical techniques (U.S. Pat. No. 6,611,634), electrochemical techniques (U. S. Pat. No. 6,632,339) and piezoelectric techniques (U. S. Pat. No. 6,566,787).

Optical transduction offers the largest number of possible subcategories of all three of the transducer classes. This is due to the fact that optical biosensors can be used for many different types of spectroscopy (e.g., absorption, fluorescence, phosphorescence, Raman, SERS, refraction, dispersion spectrometry, etc.) with different spectrochemical properties recorded. These properties include: amplitude, energy, polarization, decay time and/or phase. One of the major advantages of optical sensors is their ability to probe surfaces and films in a non-destructive way. Additionally, they offer advantages in speed, safety, sensitivity and permitting *in situ* sensing and real time measurements. The disadvantage of optical sensor lies on that it requires external hardware for the detection of optical information, and such hardware is commonly very expensive.

Electrochemical detection is another possible means of transduction that has been used in biosensors. This technique is complementary to the optical detection methods such as fluorescence, the most sensitive of the optical techniques. Since many analytes of interest are not strongly fluorescent and tagging a molecule with a fluorescent label is often labor intensive, electrochemical transduction can be very useful. In addition, electrochemical biosensor also has advantages of low cost, fast detection and easily integrated, etc. The disadvantage is the lower sensitivity of this method in contrast to optical detection.

Piezoelectrics are materials that may be brought into resonance by the application of an external alternating electric field. The frequency of the resulting oscillation is determined by the mass of the crystal. By coating a piezoelectric with an appropriate biomolecule such as an antibody, these kinds of biosensors can directly detect the binding of the corresponding analyte. Piezoelectric transducers may adopt two modes as follows:

(i) Bulk acoustic (BA) devices where adsorption of the analytes occurs on the coated surface of a piezoelectric crystal connected to an oscillator circuit. Resonance occurs in the entire mass of the crystal. If an antibody-coated crystal is placed in an atmosphere containing the selected analyte, the immunoreaction will produce an increase in the mass of the crystal. The resonant frequency will therefore decrease according to the Sauerbrey equation: $\Delta f = -2.3\times10^{6} f^{2}(\Delta m / A)$, where f is the oscillation frequency in Hz, Δm is the adsorbed mass in g, and A is the sensing area in cm^2.

(ii) Surface acoustic wave (SAW) devices where an acoustic wave moves just on the surface of the crystal. Mass loading on the acoustic path between two sets of electrodes will alter the phase wave velocity and cause a shift in the frequency.

The advantages of using piezoelectric transducer are their ease of use, ready availability and cost effectiveness. The fragility of the piezoelectric thin film undermines its applications.

Ferroelectric films are good candidates for applications such as advanced Dynamic Random Access Memory (DRAM), uncooled infrared detectors and microwave devices, because they have the advantages such as low leakage current, paraelectric room temperature with a high dielectric constant, and large dielectric breakdown strength.

One of the applications for ferroelectric film is its utility for hydrogen gas sensor. Zhu, Tan et al. [1,2] were the first to fabricate hydrogen gas sensors using ferroelectric films with a polarization potential as large as 4.5 V at 1000 ppm H_2 in air. They prepared the ferroelectric film by the sol-gel method and studied the *I-V* behavior of this type of sensor in air and in different concentrations of H_2 gas mixed in air. The data reported by Zhu, Tan and co-workers gave strong supporting evidence as to the advantage of using ferroelectric films over the conventional low dielectric constant materials in this type of device.

DESCRIPTION OF INVENTION

The object of the present invention is to use ferroelectric films for biological sensing and detection applications. The ferroelectric film serves as the transducer, and the fabricated device produces an electrical signal as the sensing output signal.

This is the first time ferroelectric material that apply the high dielectric polarization principle as the transduction method, is explored for the biosensor applications. (The current methods found in literatures are the optical techniques, electrochemical techniques, piezoelectric techniques and mass-sensitive techniques.)

The ferroelectric films, based on either thin or thick film deposition process, include but not limited to $Ba_xSr_{1-x}TiO_3$ (BST), with or without doping element (example Lanthanum), are good transducers for the biological sensing and detection applications. The films can be in the amorphous, nano-structured or polycrystalline phases. The types of biological samples include protein, DNA, virus, antigen-antibody, bacteria, fungus, etc.

The electrical signal can be either dc or ac that produces a quantifiable sensing output signal change in the presence of the biological sample with respect to the original

signal without the biological sample. The two signals can be measured sequentially or simultaneously in the application. With the introduction of a biological sample that is electrically charged or polarized in the presence of an electric field, the ferroelectric film that acts as the transducer is induced with a high dielectric polarization effect. This gives rise to a change in the original electrical signal. FIG 1 details the characterization set up for such electrical measurements. This change is in direct co-relationship with the biological sample type and its concentration or population level, and can be quantified accordingly as outlined in FIG 2.

As a new transduction method that utilizes the ferroelectric film, the current invention provides a supplement to the prior art discussed above. Compared with the conventionally used transduction method, the current invention has advantages of low cost, simple structure and short response time, etc. Moreover, the transducer can be miniaturized on the silicon wafer, and hence it can easily be put into mass production with the mature semiconductor technology process. Such miniaturization allows for the ease of construction of sensor arrays that can be used for multiple biological sample sensing and detection simultaneously with micro-fluidic channeling technique as well as integration with peripheral electronics circuitry for further signal processing of the electrical output signals such as the filtering out of background noises and quick analyte identification.

The biological samples can be applied to the sensor device and/or sensor array using the standard available immobilization technique, including the biological, chemical or plasma immobilization techniques on such ferroelectric films that are inorganic in nature.

The following describes an example of the simple device structure constructed for this invention.

DESCRIPTION OF AN EXAMPLE

The detailed description particularly refers to the accompanying figures in which:

FIG. 3 schematically shows the BST thin film transducer.

FIG. 4 shows the relationship between the measured electrical voltage shift and leakage current variations and the Bovine Serum Albumin (BSA) concentration

applied on the BST thin film. The sensing experiment results show that with higher concentration of BSA, the device shows higher electrical voltage shift and leakage current. The voltage shift at BSA concentration of 40mg/ml is about 3.2V.

COMMERCIAL APPLICATIONS

The method of sensing and detection can be applied any biological sensing instrumentation whether they are lab based instrumentations or portable instrumentations for field applications. Of greater potential commercial application is a portable instrumentation to be brought to the patient for diagnosis of a patient's condition using the patient's body fluid, such as saliva, blood, perspiration, urine etc. This type of instrumentation becomes critical in battlefield condition or in remote areas where medical diagnostic facilities are not easily accessible. The method disclosed here forms the background Intellectual Property where further work can be done to use this method to detecting concentrations of analytes or the presence of virus.

CLAIMS

We claim:

1. A method of measuring concentration of biological samples using ferroelectric film as the transducer.
2. A method of detecting biological samples using ferroelectric film as the transducer.
3. A method according to claim 1 or claim 2, in which the types of biological samples include protein, DNA, virus, antigen-antibody, bacteria, fungus.

Reference Cited

U.S. Patent Documents

6,566,787	May, 2003	Tsukahara , et al.
6,611,634	Aug., 2003	Herron, et al.
6,632,339	Oct., 2003	Bienvenut, et al.

Other References

[1] W. Zhu, O. K. Tan, J. Deng and J. T. Oh, Preparation, property, and mechanism studies of amorphous ferroelectric (Ba,Sr)TiO_3 thin films for novel metal-ferroelectric-metal type hydrogen gas sensors, *J. Mater. Res.*, **15** 1291 (2000).

[1] W. Zhu, O. K. Tan and X. Yao, "Amorphous ferroelectric $(Ba_{0.67}Sr_{0.33})Ti_{1.02}O_3$ thin films with enhanced H_2 induced interfacial polarization potential", *J. Appl. Phys.*, **84** 5134 (1998).

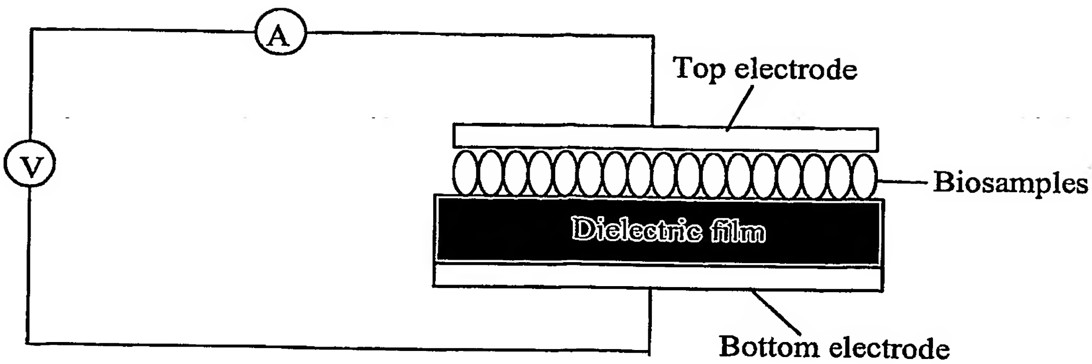


FIG. 1

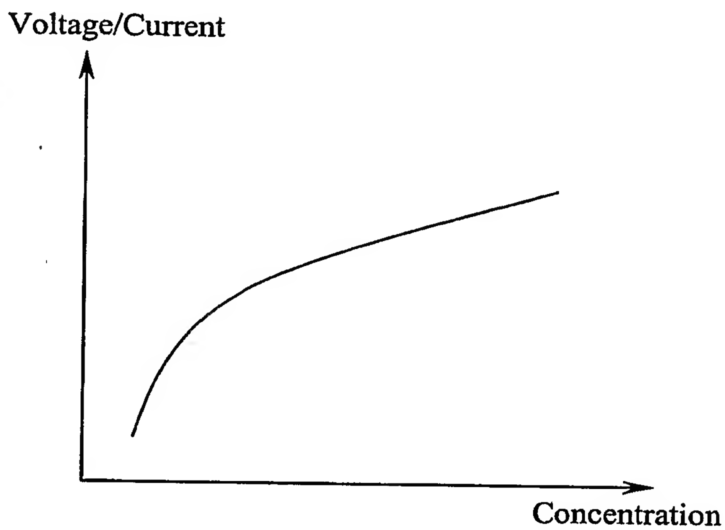


FIG. 2

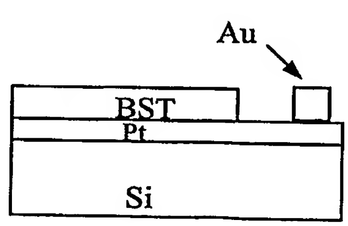
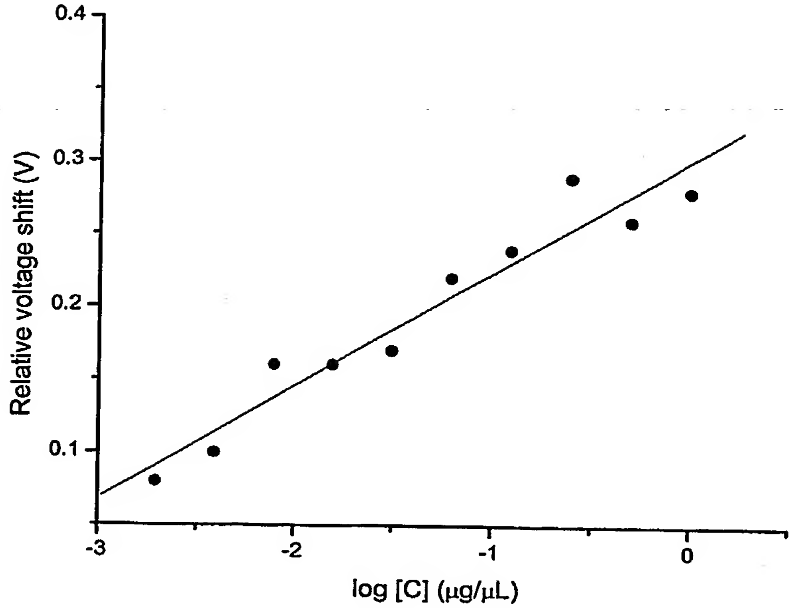
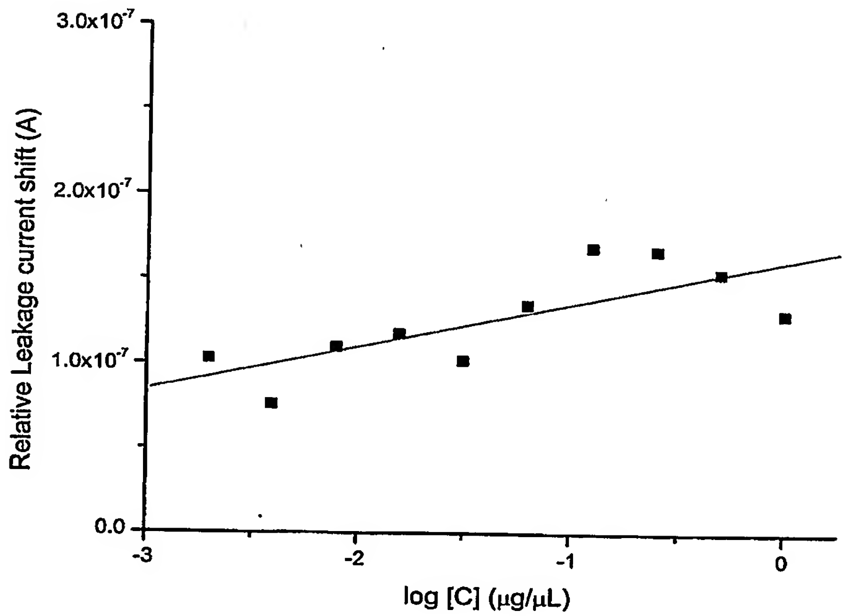


FIG. 3



Variation of relative voltage shift with BSA concentration at leakage current 0.4μA



Variation of leakage current shift with BSA concentration at voltage 0.5V

FIG. 4